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PATENT

# IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Ashkenazi et al.

Serial No.: 09/903,925

Filed: July 11, 2001

For: SECRETED AND

TRANSMEMBRANE

POLYPEPTIDES AND NUCLEIC.

**ACIDS** 

Group Art Unit: 1647

Examiner: Fozia Hamid

CERTIFICATE OF MAILING

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Date

# DECLARATION OF AUDREY D. GODDARD, Ph.D UNDER 37 C.F.R. § 1.132

Assistant Commissioner of Patents Washington, D.C. 20231

Sir:

- I, Audrey D. Goddard, Ph.D. do hereby declare and say as follows:
- I am a Senior Clinical Scientist at the Experimental Medicine/BioOncology, Medical Affairs Department of Genentech, Inc., South San Francisco, California 94080.
- 2. Between 1993 and 2001, I headed the DNA Sequencing Laboratory at the Molecular Biology Department of Genentech, Inc. During this time, my responsibilities included the identification and characterization of genes contributing to the oncogenic process, and determination of the chromosomal localization of novel genes.
- 3. My scientific Curriculum Vitae, including my list of publications, is attached to and forms part of this Declaration (Exhibit A).

Serial No.: \*
Filed: \*

- 4. I am familiar with a variety of techniques known in the art for detecting and quantifying the amplification of oncogenes in cancer, including the quantitative TaqMan PCR (i.e., "gene amplification") assay described in the above captioned patent application.
- 5. The TaqMan PCR assay is described, for example, in the following scientific publications: Higuchi *et al.*, Biotechnology 10:413-417 (1992) (Exhibit B), Livak *et al.*, PCR Methods Appl., 4:357-362 (1995) (Exhibit C) and Heid *et al.*, Genome Res. 6:986-994 (1996) (Exhibit D). Briefly, the assay is based on the principle that successful PCR yields a fluorescent signal due to Taq DNA polymerase-mediated exonuclease digestion of a fluorescently labeled oligonucleotide that is homologous to a sequence between two PCR primers. The extent of digestion depends directly on the amount of PCR, and can be quantified accurately by measuring the increment in fluorescence that results from decreased energy transfer. This is an extremely sensitive technique, which allows detection in the exponential phase of the PCR reaction and, as a result, leads to accurate determination of gene copy number.
- 6. The quantitative fluorescent TaqMan PCR assay has been extensively and successfully used to characterize genes involved in cancer development and progression. Amplification of protooncogenes has been studied in a variety of human tumors, and is widely considered as having etiological, diagnostic and prognostic significance. This use of the quantitative TaqMan PCR assay is exemplified by the following scientific publications: Pennica et al., Proc. Natl. Acad. Sci. USA 95(25):14717-14722 (1998) (Exhibit E); Pitti et al., Nature 396(6712):699-703 (1998) (Exhibit F) and Bieche et al., Int. J. Cancer 78:661-666 (1998) (Exhibit G), the first two of which I am co-author. In particular, Pennica et al. have used the quantitative TaqMan PCR assay to study relative gene amplification of WISP and c-myc in various cell lines, colorectal tumors and normal mucosa. Pitti et al. studied the genomic amplification of a decoy receptor for Fas ligand in lung and colon cancer, using the quantitative TaqMan PCR assay. Bieche et al. used the assay to study gene amplification in breast cancer.

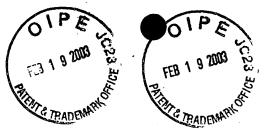
Serial No.: \*
Filed: \*

- 7. It is my personal experience that the quantitative TaqMan PCR technique is technically sensitive enough to detect at least a 2-fold increase in gene copy number relative to control. It is further my considered scientific opinion that an at least 2-fold increase in gene copy number in a tumor tissue sample relative to a normal (i.e., non-tumor) sample is significant and useful in that the detected increase in gene copy number in the tumor sample relative to the normal sample serves as a basis for using relative gene copy number as quantitated by the TaqMan PCR technique as a diagnostic marker for the presence or absence of tumor in a tissue sample of unknown pathology. Accordingly, a gene identified as being amplified at least 2-fold by the quantitative TaqMan PCR assay in a tumor sample relative to a normal sample is useful as a marker for the diagnosis of cancer, for monitoring cancer development and/or for measuring the efficacy of cancer therapy.
- 8. I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true. I declare that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Van. 16, 2003

Date

Audrey D. Goddard, Ph.D.



**PATENT** 

# IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| Applicant | :  | * |   | )      | Group Art Unit *   |
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| Appl. No. | :  | * |   | )<br>) | I hereby certify that this correspondence<br>and all marked attachments are being<br>deposited with the United States Postal |
| Filed     | :, | * |   | )      | Service as first-class mail in an envelope<br>addressed to: United States Patent and<br>Trademark Office, P.O. Box 2327,     |
| For       | :  | * |   | )      | Arlington, VA 22202, on  December 4, 2002  |
| Examiner  | :  | * | • | )      | (Date)   |
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# DECLARATION OF AUDREY D. GODDARD, Ph.D UNDER 37 C.F.R. § 1.132

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Assistant Commissioner for Patents Washington, D.C. 20231

MAR 0,3 2003

Dear Sir:

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- I, Audrey D. Goddard, Ph.D. do hereby declare and say as follows:
- 1. I am a Senior Clinical Scientist at the Experimental Medicine/BioOncology, Medical Affairs Department of Genentech, Inc., South San Francisco, California 94080.
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- 3. My scientific Curriculum Vitae, including my list of publications, is attached to and forms part of this Declaration (Exhibit A).
- 4. I am familiar with a variety of techniques known in the art for detecting and quantifying the amplification of oncogenes in cancer, including the TaqMan™ PCR assay.
- 5. The TaqMan<sup>™</sup> PCR assay is described, for example, in the following scientific publications: Higuchi *et al.*, *Biotechnology* 10:413-417 (1992) (Exhibit B); Livak *et al.*, *PCR Methods Appl.*, 4:357-362 (1995) (Exhibit C); and Heid *et al.*, *Genome Res.* 6:986-994 (1996)

Appl. No. Filed

(Exhibit D). Briefly, the assay is based on the principle that successful PCR yields a fluorescent signal due to Taq DNA polymerase-mediated exonuclease digestion of a fluorescently labeled oligonucleotide that is homologous to a sequence between two PCR primers. The extent of digestion depends directly on the amount of PCR, and can be quantified accurately be measuring the increment in fluorescence that results from decreased energy transfer. This is a sensitive technique, which allows detection in the exponential phase of the PCR and, as a result, leads to accurate determination of initial genomic sequence copy number.

- 6. The quantitative fluorescent TaqMan<sup>™</sup> PCR assay has been extensively and successfully used to characterize genes involved in cancer development and progression. Amplification of protooncogens has been studied in a variety of human tumors, and is generally considered as having etiological, diagnostic and prognostic significance. This use of the TaqMan<sup>™</sup> PCR assay is exemplified by the following scientific publications: Pennica D, *et al.*, *Proc. Natl. Acad. Sci. USA*. 95(25): 14717-14722 (1998) (Exhibit E); Pitti *et al.*, *Nature* 396(6712): 699-703 (1998) (Exhibit F); and Bieche, *et al.*, *Int. J. Cancer* 78:661-666 (1998) (Exhibit G), the first two of which I am co-author. In particular, Pennica *et al.* has used the TaqMan<sup>™</sup> PCR assay to study relative gene amplification of WISP and *c-myc* in various cell lines, colorectal tumors, and normal mucosa. Pitti *et al.* studied the genomic amplification of a decoy receptor for Fas ligand in lung and colon cancer, using the TaqMan<sup>™</sup> PCR assay. Bieche *et al.* used the assay to study gene amplification in breast cancer.
- 7. It is my personal experience that TaqMan<sup>TM</sup> PCR is technically sensitive enough to detect at least 2-fold gene amplifications relative to control. It is further my considered scientific opinion that 4-fold amplification of a gene is significant, and that at least 4-fold amplification of a gene in a tumor sample relative to control in a significant proportion of tumors is an indication that the gene is likely to be associated with malignancy. Accordingly, a gene identified as amplified at least 4-fold by the TaqMan<sup>TM</sup> technique may find utility in the diagnosis of cancer or to monitor cancer development, or the efficacy of cancer therapy.
- 8. I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true. I declare that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United

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# AUDREY D. GODDARD, Ph.D.

Genentech, Inc. 1 DNA Way South San Francisco, CA, 94080 650.225.6429 goddarda@gene.com

110 Congo St. San Francisco, CA, 94131 415.841.9154 415.819.2247 (mobile) agoddard@pacbell.net

### PROFESSIONAL EXPERIENCE

Genentech, Inc. South San Francisco, CA 1993-present

**2001 - present** Senior Clinical Scientist Experimental Medicine / BioOncology, Medical Affairs

# Responsibilities:

- Companion diagnostic oncology products
- · Acquisition of clinical samples from Genentech's clinical trials for translational research
- Translational research using clinical specimen and data for drug development and diagnostics
- Member of Development Science Review Committee, Diagnostic Oversight Team, 21 CFR Part 11 Subteam

#### Interests:

- Ethical and legal implications of experiments with clinical specimens and data
- Application of pharmacogenomics in clinical trials

#### 1998 - 2001 Senior Scientist

Head of the DNA Sequencing Laboratory, Molecular Biology Department, Research

#### Responsibilities:

- Management of a laboratory of up to nineteen –including postdoctoral fellow, associate scientist, senior research associate and research assistants/associate levels
- Management of a \$750K budget
- DNA sequencing core facility supporting a 350+ person research facility.
- DNA sequencing for high throughput gene discovery, ESTs, cDNAs, and constructs
- Genomic sequence analysis and gene identification
- DNA sequence and primary protein analysis

#### Research:

- Chromosomal localization of novel genes
- Identification and characterization of genes contributing to the oncogenic process
- Identification and characterization of genes contributing to inflammatory diseases
- Design and development of schemes for high throughput genomic DNA sequence analysis
- Candidate gene prediction and evaluation

## 1993 - 1998 Scientist

Head of the DNA Sequencing Laboratory, Molecular Biology Department, Research

# Responsibilities

- DNA sequencing core facility supporting a 350+ person research facility
- Assumed responsibility for a pre-existing team of five technicians and expanded the group into fifteen, introducing a level of middle management and additional areas of research
- Participated in the development of the basic plan for high throughput secreted protein discovery program – sequencing strategies, data analysis and tracking, database design
- High throughput EST and cDNA sequencing for new gene identification.
- Design and implementation of analysis tools required for high throughput gene identification.
- Chromosomal localization of genes encoding novel secreted proteins.

#### Research:

- Genomic sequence scanning for new gene discovery.
- Development of signal peptide selection methods.
- Evaluation of candidate disease genes.
- Growth hormone receptor gene SNPs in children with Idiopathic short stature

# Imperial Cancer Research Fund London, UK with Dr. Ellen Solomon

1989-1992

### 6/89 -12/92 Postdoctoral Fellow

- Cloning and characterization of the genes fused at the acute promyelocytic leukemia translocation breakpoints on chromosomes 17 and 15.
- Prepared a successfully funded European Union multi-center grant application

# McMaster University Hamilton, Ontario, Canada with Dr. G. D. Sweeney

1983

#### 5/83 - 8/83: NSERC Summer Student

• In vitro metabolism of β-naphthoflavone in C57BI/6J and DBA mice

## **EDUCATION**

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"Phenotypic and genotypic effects of mutations in the human retinoblastoma gene."

Supervisor: Dr. R. A. Phillips

University of Toronto Toronto, Ontario, Canada. Department of Medical

Biophysics.

1989

Honours B.Sc "The *in vitro* metabolism of the cytochrome P-448 inducer β-naphthoflavone in C57BL/6J mice."

Supervisor: Dr. G. D. Sweeney

McMaster University, Hamilton, Ontario, Canada. Department of Biochemistry

1983

#### **ACADEMIC AWARDS**

| Imperial Cancer Research Fund Postdoctoral Fellowship     | 1989-1992 |
|---|-----------|
| Medical Research Council Studentship                      | 1983-1988 |
| NSERC Undergraduate Summer Research Award                 | 1983      |
| Society of Chemical Industry Merit Award (Hons. Biochem.) | 1983      |
| Dr. Harry Lyman Hooker Scholarship                        | 1981-1983 |
| J.L.W. Gill Scholarship                                   | 1981-1982 |
| Business and Professional Women's Club Scholarship        | 1980-1981 |
| Wyerhauser Foundation Scholarship                         | 1979-1980 |

## **INVITED PRESENTATIONS**

Genentech's gene discovery pipeline: High throughput identification, cloning and characterization of novel genes. Functional Genomics: From Genome to Function, Litchfield Park, AZ, USA. October 2000

High throughput identification, cloning and characterization of novel genes. G2K:Back to Science, Advances in Genome Biology and Technology I. Marco Island, FL, USA. February 2000

Quality control in DNA Sequencing: The use of Phred and Phrap. Bay Area Sequencing Users Meeting, Berkeley, CA, USA. April 1999

High throughput secreted protein identification and cloning. Tenth International Genome Sequencing and Analysis Conference, Miami, FL, USA. September 1998

The evolution of DNA sequencing: The Genentech perspective. Bay Area Sequencing Users Meeting, Berkeley, CA, USA. May 1998

Partial Growth Hormone Insensitivity: The role of GH-receptor mutations in Idiopathic Short Stature. Tenth Annual National Cooperative Growth Study Investigators Meeting, San Francisco, CA, USA. October, 1996

Growth hormone (GH) receptor defects are present in selected children with non-GH-deficient short stature: A molecular basis for partial GH-insensitivity. 76<sup>th</sup> Annual Meeting of The Endocrine Society, Anaheim, CA, USA. June 1994

A previously uncharacterized gene, myl, is fused to the retinoic acid receptor alpha gene in acute promyelocytic leukemia. XV International Association for Comparative Research on Leukemia and Related Disease, Padua, Italy. October 1991

### **PATENTS**

Goddard A, Godowski PJ, Gurney AL. NL2 Tie ligand homologue polypeptide. Patent Number: 6,455,496. Date of Patent: Sept. 24, 2002.

**Goddard A**, Godowski PJ and Gurney AL. NL3 Tie ligand homologue nucleic acids. Patent Number: 6,426,218. Date of Patent: July 30, 2002.

Godowski P, Gurney A, Hillan KJ, Botstein D, **Goddard A**, Roy M, Ferrara N, Tumas D, Schwall R. NL4 Tie ligand homologue nucleic acid. Patent Number: 6,4137,770. Date of Patent: July 2, 2002.

Ashkenazi A, Fong S, **Goddard A**, Gurney AL, Napier MA, Tumas D, Wood WI. Nucleic acid encoding A-33 related antigen poly peptides. Patent Number: 6,410,708. Date of Patent:: Jun. 25, 2002.

Botstein DA, Cohen RL, **Goddard AD**, Gurney AL, Hillan KJ, Lawrence DA, Levine AJ, Pennica D, Roy MA and Wood WI. WISP polypeptides and nucleic acids encoding same. Patent Number: 6,387,657. Date of Patent: May 14, 2002.

**Goddard A**, Godowski PJ and Gurney AL. Tie ligands. Patent Number: 6,372,491. Date of Patent: April 16, 2002.

Godowski PJ, Gurney AL, **Goddard A** and Hillan K. TIE ligand homologue antibody. Patent Number: 6,350,450. Date of Patent: Feb. 26, 2002.

Fong S, Ferrara N, **Goddard** A, Godowski PJ, Gurney AL, Hillan K and Williams PM. Tie receptor tyrosine kinase ligand homologues. Patent Number: 6,348,351. Date of Patent: Feb. 19, 2002.

**Goddard A**, Godowski PJ and Gurney AL. Ligand homologues. Patent Number: 6,348,350. Date of Patent: Feb. 19, 2002.

Attie KM, Carlsson LMS, Gesundheit N and **Goddard A**. Treatment of partial growth hormone insensitivity syndrome. Patent Number: 6,207,640. Date of Patent: March 27, 2001.

Fong S, Ferrara N, **Goddard A**, Godowski PJ, Gurney AL, Hillan K and Williams PM. Nucleic acids encoding NL-3. Patent Number: 6,074,873. Date of Patent: June 13, 2000

Attie K, Carlsson LMS, Gesunheit N and **Goddard A**. Treatment of partial growth hormone insensitivity syndrome. Patent Number: 5,824,642. Date of Patent: October 20, 1998

Attie K, Carlsson LMS, Gesunheit N and **Goddard A**. Treatment of partial growth hormone insensitivity syndrome. Patent Number: 5,646,113. Date of Patent: July 8, 1997

Multiple additional provisional applications filed

# **PUBLICATIONS**

Seshasayee D, Dowd P, Gu Q, Erickson S, **Goddard AD** Comparative sequence analysis of the *HER2* locus in mouse and man. Manuscript in preparation.

Abuzzahab MJ, **Goddard A**, Grigorescu F, Lautier C, Smith RJ and Chernausek SD. Human IGF-1 receptor mutations resulting in pre- and post-natal growth retardation. Manuscript in preparation.

Aggarwal S, Xie, M-H, Foster J, Frantz G, Stinson J, Corpuz RT, Simmons L, Hillan K, Yansura DG, Vandlen RL, **Goddard AD** and Gurney AL. FHFR, a novel receptor for the fibroblast growth factors. Manuscript submitted.

Adams SH, Chui C, Schilbach SL, Yu XX, **Goddard AD**, Grimaldi JC, Lee J, Dowd P, Colman S., Lewin DA. (2001) BFIT, a unique acyl-CoA thioesterase induced in thermogenic brown adipose tissue: Cloning, organization of the human gene, and assessment of a potential link to obesity. *Biochemical Journal* **360**: 135-142.

Lee J. Ho WH. Maruoka M. Corpuz RT. Baldwin DT. Foster JS. **Goddard AD**. Yansura DG. Vandlen RL. Wood WI. Gurney AL. (2001) IL-17E, a novel proinflammatory ligand for the IL-17 receptor homolog IL-17Rh1. *Journal of Biological Chemistry* **276**(2): 1660-1664.

Xie M-H, Aggarwal S, Ho W-H, Foster J, Zhang Z, Stinson J, Wood WI, **Goddard AD** and Gurney AL. (2000) Interleukin (IL)-22, a novel human cytokine that signals through the interferon-receptor related proteins CRF2-4 and IL-22R. *Journal of Biological Chemistry* **275**: 31335-31339.

Weiss GA, Watanabe CK, Zhong A, **Goddard A** and Sidhu SS. (2000) Rapid mapping of protein functional epitopes by combinatorial alanine scanning. *Proc. Natl. Acad. Sci. USA* **97**: 8950-8954.

Guo S, Yamaguchi Y, Schilbach S, Wada T.;Lee J, **Goddard A**, French D, Handa H, Rosenthal A. (2000) A regulator of transcriptional elongation controls vertebrate neuronal development. *Nature* **408**: 366-369.

Yan M, Wang L-C, Hymowitz SG, Schilbach S, Lee J, **Goddard A**, de Vos AM, Gao-WQ, Dixit VM. (2000) Two-amino acid molecular switch in an epithelial morphogen that regulates binding to two distinct receptors. *Science* **290**: 523-527.

Sehl PD, Tai JTN, Hillan KJ, Brown LA, **Goddard A**, Yang R, Jin H and Lowe DG. (2000) Application of cDNA microarrays in determining molecular phenotype in cardiac growth, development, and response to injury. *Circulation* **101**: 1990-1999.

Guo S, Brush J, Teraoka H, **Goddard A**, Wilson SW, Mullins MC and Rosenthal A. (1999) Development of noradrenergic neurons in the zebrafish hindbrain requires BMP, FGF8, and the homeodomain protein soulless/Phox2A. *Neuron* **24**: 555-566.

Stone D, Murone, M, Luoh, S, Ye W, Armanini P, Gurney A, Phillips HS, Brush, J, **Goddard A**, de Sauvage FJ and Rosenthal A. (1999) Characterization of the human suppressor of fused; a negative regulator of the zinc-finger transcription factor Gli. *J. Cell Sci.* **112**: 4437-4448.

Xie M-H, Holcomb I, Deuel B, Dowd P, Huang A, Vagts A, Foster J, Liang J, Brush J, Gu Q, Hillan K, **Goddard A** and Gurney, A.L. (1999) FGF-19, a novel fibroblast growth factor with unique specificity for FGFR4. *Cytokine* **11**: 729-735.

Yan M, Lee J, Schilbach S, **Goddard A** and Dixit V. (1999) mE10, a novel caspase recruitment domain-containing proapoptotic molecule. *J. Biol. Chem.* **274**(15): 10287-10292.

Gurney AL, Marsters SA, Huang RM, Pitti RM, Mark DT, Baldwin DT, Gray AM, Dowd P, Brush J, Heldens S, Schow P, **Goddard AD**, Wood WI, Baker KP, Godowski PJ and Ashkenazi A. (1999) Identification of a new member of the tumor necrosis factor family and its receptor, a human ortholog of mouse GITR. *Current Biology* **9**(4): 215-218.

Ridgway JBB, Ng E, Kern JA, Lee J, Brush J, **Goddard A** and Carter P. (1999) Identification of a human anti-CD55 single-chain Fv by subtractive panning of a phage library using tumor and nontumor cell lines. *Cancer Research* 59: 2718-2723.

Pitti RM, Marsters SA, Lawrence DA, Roy M, Kischkel FC, Dowd P, Huang A, Donahue CJ, Sherwood SW, Baldwin DT, Godowski PJ, Wood WI, Gurney AL, Hillan KJ, Cohen RL, **Goddard AD**, Botstein D and Ashkenazi A. (1998) Genomic amplification of a decoy receptor for Fas ligand in lung and colon cancer. *Nature* **396**(6712): 699-703.

Pennica D, Swanson TA, Welsh JW, Roy MA, Lawrence DA, Lee J, Brush J, Taneyhill LA, Deuel B, Lew M, Watanabe C, Cohen RL, Melhem MF, Finley GG, Quirke P, **Goddard AD**, Hillan KJ, Gurney AL, Botstein D and Levine AJ. (1998) WISP genes are members of the connective tissue growth factor family that are up-regulated in wnt-1-transformed cells and aberrantly expressed in human colon tumors. *Proc. Natl. Acad. Sci. USA*. **95**(25): 14717-14722.

Yang RB, Mark MR, Gray A, Huang A, Xie MH, Zhang M, **Goddard A**, Wood WI, Gurney AL and Godowski PJ. (1998) Toll-like receptor-2 mediates lipopolysaccharide-induced cellular signalling. *Nature* **395**(6699): 284-288.

Merchant AM, Zhu Z, Yuan JQ, **Goddard A**, Adams CW, Presta LG and Carter P. (1998) An efficient route to human bispecific IgG. *Nature Biotechnology* **16**(7): 677-681.

Marsters SA, Sheridan JP, Pitti RM, Brush J, **Goddard A** and Ashkenazi A. (1998) Identification of a ligand for the death-domain-containing receptor Apo3. *Current Biology* **8**(9): 525-528.

Xie J, Murone M, Luoh SM, Ryan A, Gu Q, Zhang C, Bonifas JM, Lam CW, Hynes M, **Goddard A**, Rosenthal A, Epstein EH Jr. and de Sauvage FJ. (1998) Activating Smoothened mutations in sporadic basal-cell carcinoma. *Nature*. **391**(6662): 90-92.

Marsters SA, Sheridan JP, Pitti RM, Huang A, Skubatch M, Baldwin D, Yuan J, Gurney A, Goddard AD, Godowski P and Ashkenazi A. (1997) A novel receptor for Apo2L/TRAIL contains a truncated death domain. *Current Biology.* **7**(12): 1003-1006.

Hynes M, Stone DM, Dowd M, Pitts-Meek S, **Goddard A**, Gurney A and Rosenthal A. (1997) Control of cell pattern in the neural tube by the zinc finger transcription factor *Gli-1*. *Neuron* **19**: 15–26.

Sheridan JP, Marsters SA, Pitti RM, Gurney A., Skubatch M, Baldwin D, Ramakrishnan L, Gray CL, Baker K, Wood WI, **Goddard AD**, Godowski P, and Ashkenazi A. (1997) Control of TRAIL-Induced Apoptosis by a Family of Signaling and Decoy Receptors. *Science* **277** (5327): 818-821.

**Goddard AD**, Dowd P, Chernausek S, Geffner M, Gertner J, Hintz R, Hopwood N, Kaplan S, Plotnick L, Rogol A, Rosenfield R, Saenger P, Mauras N, Hershkopf R, Angulo M and Attie, K. (1997) Partial growth hormone insensitivity: The role of growth hormone receptor mutations in idiopathic short stature. *J. Pediatr.* **131**: S51-55.

Klein RD, Sherman D, Ho WH, Stone D, Bennett GL, Moffat B, Vandlen R, Simmons L, Gu Q, Hongo JA, Devaux B, Poulsen K, Armanini M, Nozaki C, Asai N, **Goddard A**, Phillips H, Henderson CE, Takahashi M and Rosenthal A. (1997) A GPI-linked protein that interacts with Ret to form a candidate neurturin receptor. *Nature*. **387**(6634): 717-21.

Stone DM, Hynes M, Armanini M, Swanson TA, Gu Q, Johnson RL, Scott MP, Pennica D, **Goddard A**, Phillips H, Noll M, Hooper JE, de Sauvage F and Rosenthal A. (1996) The tumour-suppressor gene patched encodes a candidate receptor for Sonic hedgehog. *Nature* **384**(6605): 129-34.

Marsters SA, Sheridan JP, Donahue CJ, Pitti RM, Gray CL, **Goddard AD**, Bauer KD and Ashkenazi A. (1996) Apo-3, a new member of the tumor necrosis factor receptor family, contains a death domain and activates apoptosis and NF-kappa β. *Current Biology* **6**(12): 1669-76.

Rothe M, Xiong J, Shu HB, Williamson K, **Goddard A** and Goeddel DV. (1996) I-TRAF is a novel TRAF-interacting protein that regulates TRAF-mediated signal transduction. *Proc. Natl. Acad. Sci. USA* **93**: 8241-8246.

Yang M, Luoh SM, **Goddard A**, Reilly D, Henzel W and Bass S. (1996) The bglX gene located at 47.8 min on the Escherichia coli chromosome encodes a periplasmic beta-glucosidase. *Microbiology* **142**: 1659-65.

**Goddard AD** and Black DM. (1996) Familial Cancer in Molecular Endocrinology of Cancer. Waxman, J. Ed. Cambridge University Press, Cambridge UK, pp.187-215.

Treanor JJS, Goodman L, de Sauvage F, Stone DM, Poulson KT, Beck CD, Gray C, Armanini MP, Pollocks RA, Hefti F, Phillips HS, **Goddard A**, Moore MW, Buj-Bello A, Davis AM, Asai N, Takahashi M, Vandlen R, Henderson CE and Rosenthal A. (1996) Characterization of a receptor for GDNF. *Nature* **382**: 80-83.

Klein RD, Gu Q, **Goddard A** and Rosenthal A. (1996) Selection for genes encoding secreted proteins and receptors. *Proc. Natl. Acad. Sci. USA* **93**: 7108-7113.

Winslow JW, Moran P, Valverde J, Shih A, Yuan JQ, Wong SC, Tsai SP, **Goddard A**, Henzel WJ, Hefti F and Caras I. (1995) Cloning of AL-1, a ligand for an Eph-related tyrosine kinase receptor involved in axon bundle formation. *Neuron* **14**: 973-981.

Bennett BD, Zeigler FC, Gu Q, Fendly B, **Goddard AD**, Gillett N and Matthews W. (1995) Molecular cloning of a ligand for the EPH-related receptor protein-tyrosine kinase Htk. *Proc. Natl. Acad. Sci. USA* **92**: 1866-1870.

Huang X, Yuang J, **Goddard A**, Foulis A, James RF, Lernmark A, Pujol-Borrell R, Rabinovitch A, Somoza N and Stewart TA. (1995) Interferon expression in the pancreases of patients with type I diabetes. *Diabetes* **44**: 658-664.

**Goddard AD**, Yuan JQ, Fairbairn L, Dexter M, Borrow J, Kozak C and Solomon E. (1995) Cloning of the murine homolog of the leukemia-associated PML gene. *Mammalian Genome* **6**: 732-737.

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